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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,231	05/15/2002	Hagen Thielcke	5686	2577
6858	7590	05/18/2005		
EXAMINER				
JUNG, UNSU				
ART UNIT		PAPER NUMBER		
1641				

DATE MAILED: 05/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/089,231	THIELECKE ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Unsu Jung	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 08 July 2002.
- 2a) This action is FINAL.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-6 is/are pending in the application.
- 4a) Of the above claim(s) 7-10 is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1-6 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) 1-10 are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)             | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____.  | 6) <input type="checkbox"/> Other: _____.                                   |

## DETAILED ACTION

### ***Election/Restrictions***

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-6, drawn to a device for characterizing spheroids.

Group II, claim(s) 7-10, drawn to method for characterizing spheroids.

The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The application contains claims to more than one of the combinations of categories of inventions set forth by 37 CFR 1.475.

### **According to 37 CFR 1.475 regarding unity of invention:**

(a) An international and a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ("requirement of unity of invention"). Where a group of invention is claimed in an application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

(b) An international or a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories:

- (1) A product and a process of specially adapted for the manufacture of said product; or
- (2) A product and a process of use of said product; or
- (3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or

- (4) A process and an apparatus or means specifically designed for carrying out the process; or
- (5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the process.

If an application contains claims to more or less than one of the combinations of categories of invention set forth in paragraph (b) above, unity of invention might not be present. Furthermore, the determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim.

Unity of invention exists only when there is a technical relationship among the claimed inventions involving one or more special technical features. The term "special technical features" is defined as meaning those technical features that define a contribution which each of the inventions considered as a whole, makes over the prior art. The determination is made based on the content of the claims as interpreted in light of the description and drawings.

Group I has the special technical feature of characterizing spheroids by measuring impedance spectroscopy of the spheroids.

Group II involves the special technical feature introducing spheroids into the constricted region of a tube to characterizing spheroids by using impedance spectroscopy.

Furthermore, Darrain et al. (*Biosenors Bioelectronics*, 19:1245) teaches that impedance spectroscopy can be used to determine antibody-antigen interaction (abstract, lines 3-4).

During a telephone conversation with Ms. Mary Breiner on March 21, 2005 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-6. Affirmation of this election must be made by applicant in replying to this

Office action. Claims 7-10 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

### ***Specification***

Applicant is reminded of the proper content of an abstract of the disclosure.

A patent abstract is a concise statement of the technical disclosure of the patent and should include that which is new in the art to which the invention pertains. If the patent is of a basic nature, the entire technical disclosure may be new in the art, and the abstract should be directed to the entire disclosure. If the patent is in the nature of an improvement in an old apparatus, process, product, or composition, the abstract should include the technical disclosure of the improvement. In certain patents, particularly those for compounds and compositions, wherein the process for making and/or the use thereof are not obvious, the abstract should set forth a process for making and/or use thereof. If the new technical disclosure involves modifications or alternatives, the abstract should mention by way of example the preferred modification or alternative.

The abstract should not refer to purported merits or speculative applications of the invention and should not compare the invention with the prior art.

Where applicable, the abstract should include the following:

- (1) if a machine or apparatus, its organization and operation;
- (2) if an article, its method of making;
- (3) if a chemical compound, its identity and use;
- (4) if a mixture, its ingredients;
- (5) if a process, the steps.

Extensive mechanical and design details of apparatus should not be given.

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The spacing of the lines of the specification is such as to make reading difficult.

New application papers with lines 1½ or double spaced on good quality paper are required.

The abstract of the disclosure is objected to because it contains more than one paragraph. Correction is required. See MPEP § 608.01(b).

The disclosure is objected to because of the following informalities: "Brief Description of Drawings" section (p7) title is missing. Appropriate correction is required.

The disclosure is objected to because of the following informalities: the word "resultss" (p4, line 41) is misspelled. Appropriate correction is required.

### ***Claim Objections***

The claims are objected to because the lines are crowded too closely together, making reading difficult. Substitute claims with lines one and one-half or double spaced on good quality paper are required. See 37 CFR 1.52(b).

Claims 4-6 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claims cannot depend from another multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims 4-6 have not been further treated on the merits.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

In claim 1, the word "its" (line 3) is vague and indefinite. It is unclear to which term the word "its" refers.

In claim 1, the phrase "to-be-characterized" is vague and indefinite. The specification does not define the phrase and it is unclear as to what the term "to-be-characterized" means.

In claim 4, the phrase "said region (1), said tube (1,2) has an inner diameter of between 0.1 and 0.5mm" is vague and indefinite. It is unclear which region has the inner diameter of between 0.1 and 0.5mm. The phrase should read "said region (1) of said tube (1,2).

In claim 6 (p1, line 3), the phrase "step-like" is vague and indefinite. The specification does not define the phrase and it is unclear as to what the term "step-like" means.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.

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3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Damay ("Rheology of Blood Cells in Sickle Cell Disease", Thesis in M.S., University of Florida, 1997) in view of Frank et al. (U.S. Patent No. 5,686,309, 1997) and Schwan et al. (The Review of Scientific Instruments, Vol. 39, pp481-485, 1968).

Damay teaches a method of modeling cell deformation by introducing a cell into a tube having an inner diameter, which is step-like and smaller than the diameter of the cell (p59, lines 16-19 and p60, Figure 5.1(a)). A fluorescent method is used to model the leukocyte rheological behavior. Damay also discloses a method of making a conically shaped tube by pulling a heated glass capillary tube, which is an electrically insulating material (p23, lines 15-17). However, Damay fails to teach a method of characterizing cell deformation by using bioelectric impedance measurement, including two pairs of electrodes.

Frank et al. teaches a method of characterizing cell deformation to measure bioelectric impedance by using an apparatus which comprises a tube (flow cell) having a constricted region with two electrodes, which are connected to a current source (current source) and a voltage source (resistance detector), inserted in the tube to measure impedance (resistance) of individual cells, deformed by means of hydrodynamic force (Sheet 1 of 7, Figure 1 and column 10, lines 59-60). Such an electrical measurement would provide an improved application that has the ability to quickly and accurately determine individual cell concentration at a lower cost with a

simpler instrument than the optical system (column 3, line 67 to column 4, line 5).

However, Frank et al. uses two electrode technique and fails to teach the use of four electrode technique to measure impedance of a deformed cell.

Schwan et al. teaches the use of bioelectric impedance techniques such as four electrode technique, in which two inner electrodes are connected to a voltage meter and two outer electrodes are connected to a current source to measure impedance of a biological sample (p482, Figure 1). Schwan et al. further teaches that for materials of relatively high conductivity, such as physiologic fluids, cell suspensions and tissues, electrode polarization cause the approximation to the voltage across the sample to weaken and at sufficiently low frequencies to fail (p487, column 1, *Introduction*, lines 6-10). Four electrode measurement techniques have been used to eliminate the problem of electrode polarization associated with two-electrode apparatus by providing a second pair of electrodes, non-current-carrying, with which to measure the voltage across the sample (p481, column 1, *Introduction*, lines 14-17).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the device of Damay, with an electrode system as taught by Frank et al. in order to determine deformation characteristics of cells by measuring bioelectric impedance of the cell under deformation quickly and accurately at a lower cost. Furthermore, it would have been obvious to one of ordinary skill in the art to employ in the device of Damay a four electrode technique as taught by Schwan et al. in order to eliminate the problem of electrode polarization associated with a two electrode system to measure bioelectric impedance of a biological sample.

With respect to claim 4, the inner diameter of Damay is dependent on the cell type because Damay teaches that the cell must flow through a constricted geometry to induce deformation of the cell in order to perform resistance measurement.

Therefore, it would have been obvious to one of ordinary skill in the art to modify the inner diameter of Damay within a particular dimension depending on the type of cells. Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233.

***Conclusion***

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Unsu Jung whose telephone number is 571-272-8506. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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